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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/464,099 12/16/99 BARRY

G MOBT: 175-2

HM22/0418

EXAMINER

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EWOLDT, G

ART UNIT	PAPER NUMBER
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*13*

1644

DATE MAILED:

04/18/01

Please find below and/or attached an Office communication concerning this application or proceeding.

**Commissioner of Patents and Trademarks**

<b>Office Action Summary</b>	Application No. <b>09/464,099</b>	Applicant(s) <b>Barry et al.</b>
	Examiner <b>G. R. Ewoldt</b>	Group Art Unit <b>1644</b>

Responsive to communication(s) filed on Feb 5, 2001

This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claims

Claim(s) 100-104 and 107 is/are pending in the application.

Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

Claim(s) 107 is/are allowed.

Claim(s) 100-104 is/are rejected.

Claim(s) \_\_\_\_\_ is/are objected to.

Claims \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All  Some\*  None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

Notice of References Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

**DETAILED ACTION**

1. Applicant previously elected Group I, Claims 100-104 and 107, and the species SEQ ID NO:3, in Paper No. 7. While Claims 100 and 101 were not examined in the previous action, because it was unclear how said claims related to the elected species, said claims would only have been examined as they read on SEQ ID NO:3. Therefore, said claims would have been included in the previous art rejection under 35 U.S.C. 102(b).

2. Applicant has amended the first paragraph of the specification to attain priority to U.S. Patent Application No. 07/576,537, filed 8/31/90. As said priority has overcome the previous art rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103(a), the species election requirement has been withdrawn.

3. Claims 100-104 and 107 are being acted upon.

4. In view of Applicant's Amendment and Remarks, filed 02/05/01, all previous rejections have been withdrawn.

5. The following are New Grounds for Rejection necessitated by Applicant's amendment, filed 02/05/01.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 100-104 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. While being enabling for:

an antibody immunoreactive with the 5-enolpyruvylshikimate-3-phosphate synthase enzyme (EPSPS) CP4 of SEQ ID NO:3,

the specification does not reasonably provide enablement for:  
an antibody immunoreactive with the EPSPS comprising the  
sequence domains of SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, or  
SEQ ID NO:40.

The specification discloses just a single, uncharacterized, antibody specific for a single EPSPS enzyme, CP4 (SEQ ID NO:3). As the CP4 epitope to which the antibody binds is undisclosed, it is unknown whether said antibody could bind any of the other disclosed EPSPS enzymes. Further, as antibodies are well-known to be highly specific, and the disclosed EPSPS enzymes are poorly conserved, the disclosed antibody would not be expected to bind the other enzymes.

Claims 100, is drawn an antibody which binds an EPSPS enzyme comprising any combination of four different degenerate sequences, i.e., literally thousands of proteins. Thus, the claim recites two limitations, first, that the antibodies encompassed by the claim bind all EPSPS variants, and second that all EPSPS variants bound by all the claimed antibodies have EPSPS enzyme function.

Regarding the antibodies, the specification provides insufficient guidance disclosing which substitutions or differences would be acceptable while retaining ligand binding activity. Colman (1994) teaches that even single amino acid changes in an antibody can "entirely abolish" an antibody-antigen interaction (see particularly page 33, column 2, paragraph 1) and that acceptable changes are virtually impossible to predict, i.e., even conservative substitutions can "abolish binding" (see particularly page 35, column 1, paragraph 1). Thus, it would require undue experimentation to practice the invention as claimed.

Regarding the EPSPS enzymes, the specification provides insufficient support, i.e., working examples, that any combination of any of the sequences encoded by SEQ ID NOS:37-40 would encode functional enzymes as recited in the claim. It is known in the art that even single amino acid changes or differences in a protein's amino acid sequence can have dramatic effects on the protein's function. For example, Lazar et al. (1988) teaches that a single amino acid change in TGF- $\alpha$  can dramatically affect the polypeptide's biological activity. Further, the reference teaches that certain amino acid positions can accept certain substitutions while other can accept different substitutions. In some cases the activity was reduced, in other cases it was ablated. Further note that the retention or loss of activity did not correlate with what would be considered

conservative versus non-conservative substitution (see particularly page 1250, Table 1). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (see pages 126-128, section 6-3A and page 230, paragraph bridging columns in particular). Skolnick et al. (2000) teaches that sequence-to-function methods are of limited value and that the methods "will increasingly fail as the protein-sequence databases become more diverse." Further, "inaccurate use of the sequence-to-function methods has led to significant function-annotation errors in the sequence databases," i.e., use of the method perpetuates larger and larger errors. As such, the practice of the claimed invention any combination of SEQ ID NOS:37-40 would be highly unpredictable and requiring of undue experimentation.

*In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of any working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification regarding both how to make the claimed invention, it would take undue trials and errors to practice the invention of the instant claims.

8. Claim 107 is allowed. Claims 102-104 would be allowable if recited as independent claims.

9. Applicant's amendments necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee

pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday and alternate Fridays from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

G.R. Ewoldt, Ph.D.  
Patent Examiner  
Technology Center 1600  
April 9, 2000

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